Effects of acute hypoxia on contractile responses of the bladder mucosa in vitro

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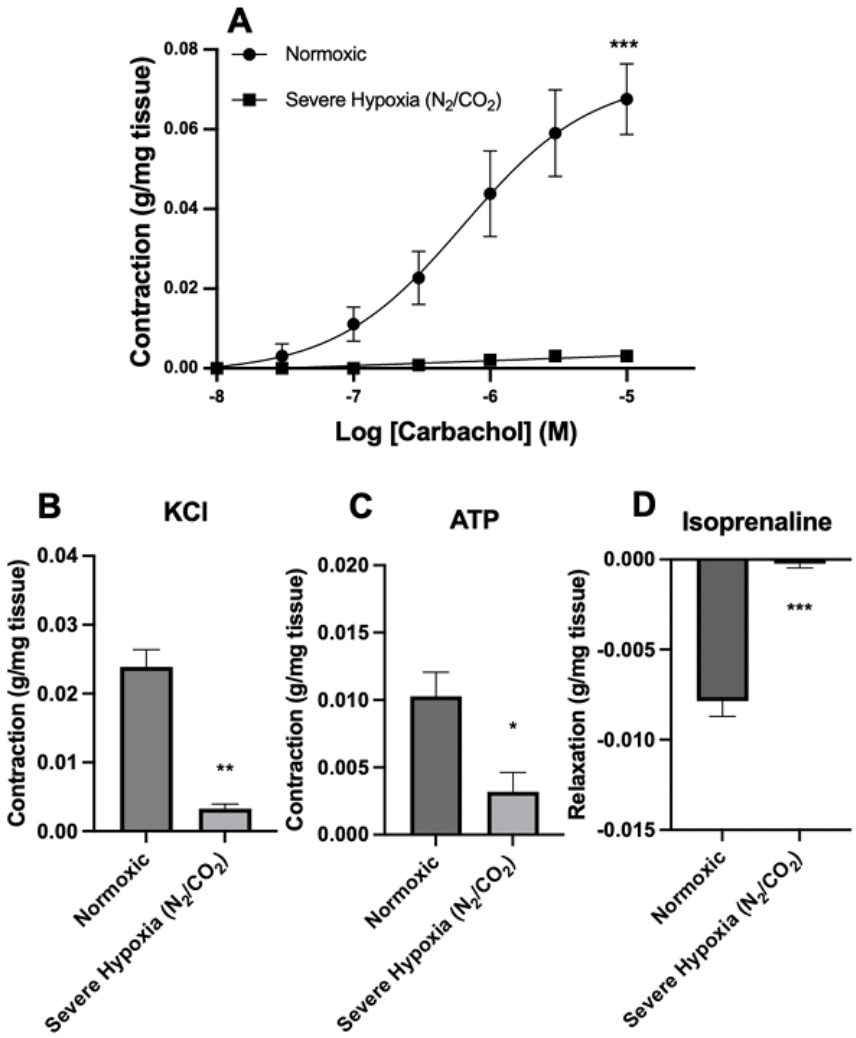
Objective: 1 in 5 adults will develop some form of bladder dysfunction throughout their lifetime, with increasing numbers in the elderly[1]. Bladder dysfunction can be characterised by an increase in urinary urgency, frequency, or having to get up from bed to urinate (nocturia).[1] Bladder dysfunction has been linked to reduced blood flow to the bladder, leading to reduced oxygen (hypoxia).[2] The bladder mucosa, which contains the inner urothelium lining and underlying lamina propria, is an important regulator of bladder function, but the consequences of hypoxia on mucosal function remains uncertain.[3] This study aimed to investigate the effects of acute hypoxia on contractile responses of the bladder mucosa in vitro.

Methods: Isolated bladder mucosa tissue strips from female porcine bladders were mounted in 8mL organ baths containing physiological Krebs-bicarbonate solution and gassed with 95% O2/5% CO2 (normoxia) for 15 minutes (maintained at ~1.5 g tension, 37˚ C). Tissues were then switched to either severe hypoxia (95% N2/5% CO2, 18 oxygen %) or mild hypoxia (95% Air/5% CO2, 100 oxygen %), with separate normoxic controls included in each experiment. Cumulative concentration responses (10nM-100μM) to the muscarinic receptor agonist, carbachol, were measured, along with responses to the β-adrenoreceptor agonist, isoprenaline (1 μM), to assess relaxation, and contractions to ATP (10 mM) and high KCl Krebs (60 mM).



Results: Severe hypoxia significantly decreased maximum contractile responses of the mucosa strips to carbachol to 5.0±1.5% of the normoxic (control) response (P<0.001, n=6), with the responses to ATP (P<0.05, n=5) and KCl (P<0.01, n=5) reduced to 32±16% and 14±3.8% of control respectively. However, the potency of carbachol was not affected by severe hypoxia (-LogEC50: control 6.19±0.25 vs severe hypoxia 6.21±0.35). The relaxation responses to isoprenaline were also attenuated (P<0.001, n=6). Mild hypoxia also significantly decreased maximum contractile responses of the mucosa to carbachol (P<0.001, n=6). Responses to ATP and KCl followed a similar trend, although there was no statistical significance. Relaxation responses to isoprenaline were also decreased under mild hypoxia, though not significantly.

Conclusion: The results demonstrate a depressant effect of acute hypoxia on relaxation as well as contractile responses of the bladder mucosa. This change is likely due to a general decrease in mucosal contractility rather than receptor specific changes. These changes may contribute to the bladder dysfunction associated with reduced blood flow and hypoxia.

References

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